

**Remarks**

Applicants request consideration on the merits of the above-referenced patent application.

**I. Amendments to the specification**

Paragraphs 8, 13, 14, 15, 20, 23, 47, 49-51, 297, 629, 974, 1350, and 1398, and the heading on page 189 (at line 1) have been amended by this preliminary amendment. Pursuant to 37 C.F.R. §1.121, replacement paragraphs are provided in the previous section on pages 2-24, and a marked up version of the amendments are provided in the attached Appendix A (pages 224-247). Applicants submit that these amendments do not introduce new matter. Specifically:

Paragraphs 8, 13, 14, 15, 20, 297, 974, 1350, and 1398 have been amended to correct various cites. These amendments correct obvious errors, and are therefore permissible under MPEP §2163.07. These amendments also are supported by the cited references themselves.

Formula (I) in paragraphs 23 and 47 has been amended to include hydrogen as an alternative to R<sup>x</sup> on the sulfonyl-bonded piperidinyl or piperazinyl. This amendment is supported by, for example, Formula (IA) on page 13. More specifically, Formula (IA) illustrates the fact that the R<sup>x</sup> substituent is an optional substituent of the sulfonyl-bonded piperidinyl or piperazinyl by defining a sub-genus of Formula (I) wherein the piperidinyl or piperazinyl does not have an R<sup>x</sup> substituent.

Formulas (IB-1), (IB-2), and (IB-5) in paragraphs 49-51 have been amended to be consistent with amended Formula (I). The amendment to Formula (IB-2) also is supported by, for example, Formula (IB-3) in paragraph 50. More specifically, Formula (IB-3) illustrates the fact that the R<sup>x</sup> substituent in Formula (IB-2) is an optional substituent of the sulfonyl-bonded piperidinyl or piperazinyl by defining a sub-genus of Formula (IB-2) wherein the piperidinyl or piperazinyl does not have an R<sup>x</sup> substituent.

Formula (360-1) in paragraph 629 has been amended to include hydrogen as an alternative to R<sup>x</sup> on the sulfonyl-bonded piperidinyl or piperazinyl. This amendment is supported by, for example, Formula (361-1) on page 187. More specifically, Formula (361-1) illustrates the fact that the R<sup>x</sup> substituent is an optional substituent on the sulfonyl-bonded piperidinyl or piperazinyl by defining a sub-genus of Formula (360-1) wherein the piperidinyl or piperazinyl does not have an R<sup>x</sup> substituent.

The heading on page 189 at line 1 has been amended to specifically characterize the selectivities as MMP selectivities. This amendment is supported by paragraphs 644-665 (on pages 189-194) that follow the heading.

Paragraphs 654 and 665 have been amended to replace "MMP-3" with "MMP-13". This amendment corrects an obvious typographical error, and is therefore proper under MPEP §2163.07. This amendment also is supported by Applicants' specification, which, for example, repeatedly indicates that selective inhibition of MMP-2, MMP-9, and MMP-13 activity is often particularly preferred when preventing or treating the diseases listed in paragraphs 654 and 665. *See, e.g.*, Paragraphs 649 and 660 on pages 190 and 192, respectively.

Paragraph 686 has been amended to include aggrecanase as a target of the compounds of this invention. This amendment is supported throughout Applicants' specification. Such support includes, for example, paragraph 35 on page 10.

Paragraph 925 has been amended to replace "hydroxamate" with "hydroxamic acid". This amendment is supported by, for example, the compound title and structure on in paragraph 920 on page 279 (which shows a hydroxamic acid as the compound ultimately being made in paragraph 925).

Other amendments simply rephrase the specification, remove redundancies or unnecessary terms, or correct grammatical or obvious errors. Such amendments are permissible under MPEP §2163.07.

## **II. Amendments to claims**

Claims 1-374 are pending. Claims 1, 20, 62, 96, 102, 105, 318, 342, 347, 353, 359 and 360 have been amended. All the claims, including the amendments, are shown in the previous section on pages 25-219. Applicants submit that the amendments do not introduce new matter. Specifically:

The chemical structures in claims 1 and 360 have been amended to include hydrogen as an alternative to R<sup>x</sup> on the sulfonyl-bonded piperidinyl or piperazinyl. This amendment is supported by, for example, claims 2 and 361 (as originally filed), which depend from claims 1 and 360, respectively. More specifically, claims 2 and 361 illustrate the fact that the R<sup>x</sup> substituent is an optional substituent on the sulfonyl-bonded piperidinyl or piperazinyl by

defining a sub-genus of claims 1 and 360 wherein the piperidinyl or piperazinyl does not have an R<sup>x</sup> substituent.

Claims 96, 102, and 105 have been amended to expressly recite the fact that the halogen substitution is partial substitution. This amendment makes the language in the claims more consistent with the language in claim 95 (*i.e.*, the claim from which claims 96, 102, and 105 directly or indirectly depend).

Claim 105 has been amended to expressly recite the fact that the halogen substitution may be one or more fluoro. This amendment makes the language more consistent with the language in claim 95 (*i.e.*, the claim from which claim 105 indirectly depends).

Claim 318 has been amended to expressly recite the fact that the E<sup>3</sup> alkyl is substituted with one or more independently selected halogen. This amendment makes the language more consistent with the language in claim 307 (*i.e.*, the claim from which claim 318 indirectly depends).

Claims 347 and 353 have been amended to expressly recite the fact that the E<sup>3</sup> alkyl is substituted with one or more independently selected halogen. This amendment makes the language in these claims more consistent with the language in claim 342 (*i.e.*, the claim from which claims 347 and 353 indirectly depend).

Other amendments simply rephrase the claims, or correct grammatical or obvious errors. Such amendments are permissible under MPEP §2163.07.

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Applicants believe that they do not owe any fee in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **08-0750**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

Preliminary Amendment A  
Appl. No. 10/618,288  
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Applicants submit that the pending claims are in condition for allowance, and request that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'D. Gryte' with a stylized flourish at the end.

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